

Preferential association between childhood emotional abuse and bipolar disorder.

Bruno Etain, Flavie Mathieu, Chantal Henry, Aurélie Raust, Isabelle Roy, Anne Germain, Marion Leboyer, Frank Bellivier

► **To cite this version:**

Bruno Etain, Flavie Mathieu, Chantal Henry, Aurélie Raust, Isabelle Roy, et al.. Preferential association between childhood emotional abuse and bipolar disorder.. *Journal of Traumatic Stress*, Wiley, 2010, 23 (3), pp.376-83. <10.1002/jts.20532>. <inserm-00497585>

HAL Id: inserm-00497585

<http://www.hal.inserm.fr/inserm-00497585>

Submitted on 27 Aug 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Preferential association between childhood emotional abuse and bipolar disorder

Journal:	<i>Journal of Traumatic Stress</i>
Manuscript ID:	JOTS-08-0280.R4
Wiley - Manuscript type:	Research Article
Date Submitted by the Author:	29-Jan-2010
Complete List of Authors:	Etain, Bruno; Hopital Albert Chenevier, Pole de Psychiatrie Mathieu, Flavie Henry, Chantal Raust, Aurelie Roy, Isabelle Germain, Anne Leboyer, Marion Bellivier, Frank
Keyword - Topics:	Etiology/risk and protective factors
Keywords - Trauma Exposure:	Sexual abuse/assault, childhood
Keyword - Statistical Categories:	
Keyword - Intervention:	
Keyword - Special Populations:	



1
2
3 Preferential association between childhood emotional abuse and bipolar disorder
4
5
6
7

8 Running head: Emotional abuse and bipolar disorder
9
10

11
12 Bruno ETAIN (1,3), Flavie MATHIEU (1), Chantal HENRY (1,2,3), Aurélie RAUST (1,3),
13
14 Isabelle ROY (3), Anne GERMAIN (4), Marion LEBOYER (1,2,3), Frank BELLIVIER (1,2,3).
15
16
17

18
19
20 1) INSERM, Unité 955, IMRB, Pôle de Génomique Médicale, Equipe de Psychiatrie Génétique,
21
22 Créteil, F-94000, France ;
23

24
25 2) Université Paris Est, Faculté de Médecine, IFR10, Créteil, F-94000, France ;
26

27 3) AP-HP, Groupe Henri Mondor-Albert Chenevier, Pôle de Psychiatrie, Créteil, F-94000,
28
29 France ;
30

31 4) Department of Psychiatry, University of Pittsburgh School of Medicine, Pennsylvania, USA.
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Corresponding author:

4
5 Bruno ETAIN, MD, PhD.

6
7 Pôle de Psychiatrie

8
9 Hôpital Albert Chenevier

10
11 40, rue de Mesly

12
13 94010 Créteil Cedex - FRANCE

14
15 Tel: + 33 1 49 81 32 90

16
17 Fax: + 33 1 49 81 30 99

18
19 Mail : bruno.etaïn@inserm.fr

20
21
22 Conflict of interest: none

23
24
25
26
27
28
29
30
31
32 Word count: 111 (abstract); 5937 (article with references, tables and figures); 4 tables; 1 figure

33
34
35
36
37
38 Acknowledgements

39
40 This work was supported by *INSERM, Assistance Publique des Hôpitaux de Paris (AP-HP),*
41
42 *Agence Nationale pour la Recherche (ANR – Project Manage-BP), Fondation pour la Recherche*
43
44 *sur le Cerveau (FRC) and RTRS Santé Mentale (Fondation FondaMental).* We thank E. Abadie,
45
46
47 C. Bulach, B. Cochet, M. Fabbro and M.J. Pereira Gomes for their assistance. We thank patients
48
49
50 and controls for their participation.
51
52
53
54
55
56
57
58
59
60

Abstract

Childhood trauma has been suggested to be involved in the susceptibility to bipolar disorder. However, case-control studies are lacking, while the preferential implication and the dose-effect of different trauma subtypes remain poorly investigated. 206 bipolar patients and 94 controls completed the Childhood Trauma Questionnaire (CTQ). The CTQ total score was higher for bipolar patients than for controls. The presence of multiple trauma was significantly more frequent in bipolar patients than in controls (63% versus 33%). Multiple logistic regression suggested that only emotional abuse was associated with bipolar disorder with a suggestive dose-effect. Clinical practice should include systematic assessment of childhood trauma among bipolar patients with a particular focus on emotional abuse.

Key words:

Bipolar disorder, childhood affective trauma, childhood trauma questionnaire, emotional abuse, dose-effect.

Introduction

Bipolar affective disorder is a chronic and severe psychiatric disorder of multifactorial origin. More than 20 years after the demonstration of its genetic component, the search for susceptibility genes is still inconclusive (Smoller & Gardner-Schuster, 2007). This may be partly explained by the under-exploration of the environmental aspects of the disease that require to be incorporated in the analysis. Psychological stressors are probably the most promising environmental determinants (Etain, Henry, Bellivier, Mathieu, & Leboyer, 2008) and have been implicated in the onset and recurrences of unipolar and bipolar affective disorders (Cohen, Hammen, Henry, & Daley, 2004; Paykel, 2003; Post, 1992). Most investigations have focused on recent major life events, implicating both acute and chronic stressors while the role of early childhood trauma remains under-explored (Johnson & Roberts, 1995; Paykel, 2003; Rush, 2003).

Childhood traumatic events are more frequently reported by bipolar than by unipolar patients (Hyun, Friedman, & Dunner, 2000). Histories of severe childhood abuse were identified in more than half of the bipolar patients (Garno, Goldberg, Ramirez, & Ritzler, 2005; Maguire, McCusker, Meenagh, Mulholland, & Shannon, 2008). Childhood traumatic events may also modulate the clinical expression of the disorder, being associated with an earlier onset of the disease (Garno et al., 2005), rapid cycling course (Garno et al., 2005; Leverich & Post, 2006), psychotic features (Hammersley et al., 2003), suicidal behavior (Brown, McBride, Bauer, & Williford, 2005; Garno et al., 2005; Leverich & Post, 2006), comorbidities with substances misuse (Brown et al., 2005; Garno et al., 2005; Leverich & Post, 2006) and with panic disorder (Brown et al., 2005). These data thus suggest that childhood trauma may be an associated risk in

1
2
3 bipolar disorder and may also influence its clinical expression and outcome (Etain et al., 2008).
4
5
6
7

8 However, many studies in this field have been hampered by methodological limitations,
9
10 particularly the absence of control groups, but also differences between assessment methods
11 (structured interview versus self-reported measure) and small samples of patients. The
12 preferential implication of some subtypes of trauma also requires further investigation since most
13 studies have considered childhood trauma as a whole or have restricted the investigation to
14 physical and/or sexual abuses (Carballo et al., 2008; Hammersley et al., 2003). Since interaction
15 between a given subtype of trauma with specific genetic factors might be the causal link to a
16 given psychiatric condition (Caspi & Moffitt, 2006), the association between bipolar disorder and
17 different subtypes of trauma requires to be formally tested. Finally, a dose-effect of trauma
18 subtypes has never been investigated in bipolar disorder although this effect has previously been
19 reported in other psychopathological conditions, such as in psychosis (Read, van Os, Morrison, &
20 Ross, 2005).
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38

39 The aims of this study were thus (i) to retrospectively assess the prevalence and the
40 severity of different subtypes of childhood trauma among euthymic bipolar patients and controls,
41 (ii) to investigate the preferential implication of some trauma subtypes and (iii) to test for their
42 dose-effect.
43
44
45
46
47
48
49

50 Method

51 Participants

52
53
54
55
56
57
58
59
60

1
2
3 Bipolar type I and type II patients (according to DSM-IV criteria (American Psychiatric
4 Association, 1994)) were recruited in two university-affiliated psychiatric departments in France
5 (Paris/Créteil and Bordeaux). Inclusion criteria for bipolar patients were age over 18 years,
6
7
8 (Paris/Créteil and Bordeaux). Inclusion criteria for bipolar patients were age over 18 years,
9
10 caucasian and normothymia defined as a Montgomery Asberg Depression Rating Scale and a
11
12 Mania Rating Scale scores below five (Bech, Rafaelsen, Kramp, & Bolwig, 1978; Montgomery
13
14 & Asberg, 1979). The control group was composed of blood donors having neither a personal nor
15
16 a familial (first-degree relatives) history of mood disorders or suicidal behavior .
17
18
19

20 21 22 Measures

23
24
25
26
27 All participants were interviewed using the French version (Preisig, Fenton, Matthey,
28
29 Berney, & Ferrero, 1999) of the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et
30
31 al., 1994) providing lifetime DSM-IV axis I diagnoses (American Psychiatric Association, 1994).
32
33 To check the inter-rater reliability for DSM-IV axis I diagnoses, the following procedure was
34
35 applied (Preisig et al., 1999). A team of interviewers (8 psychologists and psychiatrists) was
36
37 trained over a four month period using videotaped interviews and supervisions with experienced
38
39 clinicians. All interviewers were blinded as to the referral diagnosis of the subject. Raters
40
41 performed interviews for the inter-rater and test-retest reliability study in a balanced way,
42
43 exchanging roles between first-interviewer, observer at the first interview, and retest interviewer.
44
45 Patients were interviewed by a member of the team in the presence of an observer (co-rater) who
46
47 simultaneously and independently completed a DIGS. At the end of the interview, interviewer
48
49 and observer independently assigned DSM-IV lifetime diagnoses. The inter-rater reliability was
50
51 computed on 136 patients from psychiatric inpatient and outpatient facilities with referral
52
53 diagnoses of bipolar disorder, major depressive disorder, schizoaffective disorder,
54
55
56
57
58
59
60

1
2
3 schizophrenia/schizophreniform disorder, alcohol or drug disorder. The inter-rater reliabilities
4
5 (kappa coefficients) we achieved for the DIGS were 0.85 for bipolar disorders (Preisig et al.,
6
7 1999) and 0.93 for major depressive disorder/dysthymia, this being consistent with the inter-rater
8
9 reliabilities of the English version (Nurnberger et al., 1994). The French version of the DIGS has
10
11 no specific section to check the presence of posttraumatic stress disorder.
12
13
14
15
16

17 Childhood traumatic events were recorded using the short version of the Childhood
18
19 Trauma Questionnaire (CTQ), a 28-item self-report measure developed by Bernstein et al.
20
21 (Bernstein et al., 1994). This questionnaire showed excellent test-retest reliability, as well as
22
23 convergent and discriminant validity with a structured trauma interview. It has been validated in
24
25 clinical and non clinical populations (Bernstein & Fink, 1998). The CTQ yields a total score
26
27 (range 25-125) that is recommended to be used as a continuous variable, and five sub-scores
28
29 (range 5-25 for each) for neglects (emotional and physical) and abuses (emotional, physical and
30
31 sexual) (recommended to be used as categorical variables). Emotional neglect refers to the failure
32
33 of caretakers to provide
34
35 basic psychological and emotional needs, such as love, encouragement, belonging and support.
36
37 Emotional abuse refers to verbal assaults on a child's sense of worth or well-being, or any
38
39 humiliating, demeaning, or threatening behavior directed toward a child by an older person.
40
41 Physical neglect refers to failure to provide basic physical needs including food, shelter, and
42
43 safety.
44
45 Physical abuse refers to bodily assaults on a child by an older person that pose a risk of, or result
46
47 in, injury. Sexual abuse refers to sexual contact or conduct between a child and an older person,
48
49 including explicit coercion.
50
51
52
53
54
55
56
57
58
59
60

1
2
3 According to the thresholds provided by Bernstein et al. (1994), each subtype of trauma
4 was categorized across a gradient of four levels of severity, from “no trauma” to ‘severe’ through
5 low and moderate. In this study, a trauma subtype was considered as present if reaching at least a
6 low level of severity. The French validated version of the CTQ was used in this study (Paquette,
7 Laporte, Bigras, & Zoccolillo, 2004). Bipolar patients’ euthymic state was checked using the
8 French versions of the Montgomery Asberg Depression Rating Scale and of the Mania Rating
9 Scale (Bech et al., 1978; Montgomery & Asberg, 1979) before the CTQ completion.
10
11
12
13
14
15
16
17
18
19
20
21

22 Procedure

23
24
25
26
27 For this study, participants who fulfilled inclusion criteria were systematically approached
28 (about 250 bipolar patients and 100 control subjects). More than 80% of approached participants
29 did agree to participate and all of them have then been included in the study. Comparisons
30 between participants and non-participants were not available since French ethical procedures do
31 not allow collecting the characteristics of non participants.
32
33
34
35
36
37
38
39
40

41 For bipolar patients, normothymia was assessed using the Montgomery Asberg
42 Depression Rating Scale and the Mania Rating Scale with scores requiring to be below five
43 (Bech, Rafaelsen, Kramp, & Bolwig, 1978; Montgomery & Asberg, 1979). Then, the DIGS was
44 completed in order to characterize bipolar disorders and psychiatric comorbidities. Controls were
45 screened for DSM-IV axis I diagnoses using the DIGS and included in this study only if they met
46 the inclusion criteria. They completed the CTQ only if they were free of personal and familial
47 (first-degree relatives) history of mood disorders (major depressive episodes or unipolar disorder)
48 or suicidal behavior and had a Montgomery Asberg Depression Rating Scale and the Mania
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Rating Scale scores below five (Bech, Rafaelsen, Kramp, & Bolwig, 1978; Montgomery &
4
5 Asberg, 1979).
6
7
8
9

10 For all participants, CTQ was completed after the completion of the DIGS. About 5% of
11
12 the questionnaires were not included in the analysis since they were not correctly completed
13
14 (missing items).
15
16
17

18
19
20 Written informed consent was obtained from all participants. Institutional review board
21
22 approval was previously obtained for this study.
23
24
25

26 27 Data analysis

28
29
30
31
32 CTQ total score was used as a continuous variable representing the global severity of
33
34 childhood trauma. Shapiro-Wilk tests were used to test whether the CTQ total scores fitted
35
36 normal distributions in each group. If scores were not normally distributed, non-parametric tests
37
38 were used and results were reported using the normal approximation of the statistic (z). Exact p-
39
40 values were estimated by simulation over 100.000 replicates. All trauma subtypes were
41
42 categorized using four levels of severity (“no trauma”, “low”, “moderate” and “severe”) as
43
44 defined by Bernstein et al. (Bernstein & Fink, 1998). The significance of differences between
45
46 groups was assessed using classical chi-squared tests for discrete variables. Spearman
47
48 correlations were used to estimate correlation between trauma subtypes. Logistic regression
49
50 (simple and multiple), crude and adjusted odds-ratio (OR) and 95% Confidence Interval (95%
51
52 CI) were used to test for an association between bipolar/control status and each trauma subtype.
53
54
55
56
57
58
59
60 The best model was selected using a classical likelihood ratio test or Akaike criterion. Cochran-

1
2
3 Armitage linearity test was used to test for an association between trauma subtypes and bipolar
4 disorder. Statistical analyses were performed using the SAS package (version 9.1.2, SAS
5 Institute®). Bonferroni's correction was used to allow for multiple testing. Given the number of
6 tests, a p-value equal or lower than 0.003 was considered as significant.
7
8
9
10
11
12
13
14

15 Results

16
17
18
19 The CTQ was completed by 206 bipolar patients (155 bipolar type I and 51 bipolar type
20 II) and by 94 control subjects. Age at interview was similar in the two groups ($M = 41.7$, $SD =$
21 12.6 years for bipolar patients and $M = 41.2$, $SD = 11.9$ years for control subjects , $z = -0.05$, ns).
22 The sex ratio (men/women) was significantly lower in the bipolar patient group than in the
23 control group (0.69 versus 1.61 , $\chi^2(1, N = 300) = 11.3$, $p = .0008$). The characteristics of the
24 samples are detailed in table 1.
25
26
27
28
29
30
31
32
33
34
35
36
37
38

39 The CTQ total score for both bipolar patients and control subjects groups did not fit
40 normal distributions (Shapiro-Wilk test $p < .0001$ for the two groups). Consequently, non
41 parametric tests were used to test for differences between bipolar patients and control subjects.
42 Age at interview and gender had no effect on CTQ total score in the two groups (data available
43 on request).
44
45
46
47
48
49

50 The CTQ total score was significantly higher for bipolar patients than for control subjects
51 (respectively $M = 43.4$, $SD = 13.5$ and $M = 36.3$, $SD = 7.4$; $z = -5.02$, $p < .0001$).
52
53
54
55
56
57
58
59
60

1
2
3 No category of trauma was more frequent for women than for men in either group, except
4
5 a trend for sexual abuse in the bipolar sample (presence in 37.7% of women versus 24.4% of men
6
7
8 $\chi^2(1, n = 206) = 6.15, p = .01$). Therefore, analyses were not stratified by gender.
9
10

11
12
13 The prevalence of each subtype of trauma are given for bipolar patients and controls in
14
15 table 2. Frequency distributions between bipolar patients and controls were significantly different
16
17 only for emotional abuse, but not for emotional neglect, physical neglect, physical abuse or
18
19 sexual abuse.
20
21

22
23
24 The presence of multiple trauma (at least 2 subtypes of at least a low intensity) was
25
26 significantly more frequent in bipolar patients than in controls (63.09% versus 32.98% ; $\chi^2(1, N =$
27
28 300) = 23.56 , $p < .0001$; OR = 3.48, 95% CI = 2.08 - 5.82). The higher the cumulative number
29
30 of trauma was, the higher the proportion of bipolar patient in a category (Cochrane-Armitage
31
32 linear tendency test $z = -4.52, p < .0001$).
33
34
35
36
37
38
39
40
41

42 The five subtypes of trauma were correlated as presented in table 3. Simple logistic
43
44 regression was performed including the five subtypes of trauma independently; then multiple
45
46 regression was used including the five subtypes of trauma (full model). Logistic regression
47
48 analysis results are presented in table 4. The best model includes only emotional abuse as an
49
50 explanatory variable. Likelihood ratio test of the full model versus emotional abuse only was
51
52 similar ($\chi^2(4, N = 300) = 6.4, ns$). Emotional abuse was associated with bipolar status when
53
54 considering the most parsimonious model ($p < .0001$).
55
56
57
58
59
60

1
2
3
4
5
6 Finally, the Cochran-Armitage linear trend showed that the higher the emotional abuse
7
8 severity was, the higher the proportion of bipolar patients in the group across the gradient of
9
10 severity, as shown in figure 1.
11
12
13

14 15 Discussion

16
17
18
19
20 Euthymic adult bipolar patients experienced more severe and more frequent childhood
21
22 traumatic events than control subjects. More than half of our bipolar sample reported childhood
23
24 trauma, this being consistent with several previous studies (Garno et al., 2005; Leverich et al.,
25
26 2002; Maguire et al., 2008). This study is the first to investigate five trauma subtypes frequency
27
28 and severity in a case-control design, and to test for their preferential implication and dose-effect.
29
30 The association between childhood trauma and bipolar disorder is mainly due to the over-
31
32 representation of emotional abuse in patients with a dose-effect relationship. This is consistent
33
34 with previous studies showing a dose-effect association between childhood trauma severity and
35
36 various psychiatric disorders during adulthood (for review see (Read et al., 2005)). Our results
37
38 thus suggest that, among trauma subtypes, emotional abuse may be preferentially associated with
39
40 bipolar disorder.
41
42
43
44
45
46
47

48 This study has several strengths: the comparison with a control group that has been
49
50 screened for personal and first-degree relatives history of psychiatric disorders and the use of a
51
52 reliable, validated trauma questionnaire that provides information about trauma frequency and
53
54 severity and allows fine-grained analysis for trauma subtypes and dose-effect. Nevertheless, this
55
56 study design also has several limitations.
57
58
59
60

1
2
3
4
5
6 First, the retrospective assessment of traumatic events during childhood may be
7
8 influenced by uncontrolled recall bias although reports on trauma by psychiatric patients were
9
10 suggested as remarkably reliable (Meyer, Muenzenmaier, Cancienne, & Struening, 1996). A
11
12 recall bias in trauma assessment due to time elapsed since exposure is unlikely in our study (no
13
14 correlation between CTQ total score and age at interview in both groups, no correlation between
15
16 CTQ total score and duration of illness or the number of major episodes among bipolar patients;
17
18 data not shown). Furthermore, the CTQ is a reliable, valid trauma questionnaire and its
19
20 psychometric properties have shown high levels of face validity, internal consistency, test-retest
21
22 validity and good convergent validity with structured interviews (Bernstein & Fink, 1998;
23
24 Bernstein et al., 1994; Bernstein et al., 2003; Paivio & Cramer, 2004). Nevertheless and ideally,
25
26 external sources of information should have been used to check validity.
27
28
29
30
31
32
33

34 In this study, the history of trauma was assessed during euthymic states in order to avoid
35
36 recall bias due to current mood symptoms that may lead to under or over report traumatic
37
38 experiences. Nevertheless, the potential influence of residual symptoms cannot be completely
39
40 ruled out. Finally, groups were not matched for gender and this may have influenced the findings,
41
42 although no effect of gender on the CTQ total score was observed.
43
44
45
46
47

48 The high prevalence and the severity of childhood emotional abuse in our sample could be
49
50 interpreted in several ways, nevertheless with caution. Emotional abuse might be regarded as a
51
52 potential risk factor for developing bipolar disorder. Indeed, childhood trauma might show long-
53
54 lasting effects on catecholamine response to psychological stress (Otte et al., 2005; Roy, 2002),
55
56 on corticotropin-releasing factor systems hyper-reactivity (Heim & Nemeroff, 2001; Heim et al.,
57
58
59
60

1
2
3 2002) and might alter function and structure of medial prefrontal cortex and hippocampus
4
5 (Bremner, 2002). All these neurobiological changes might lead to inadequate emotional
6
7 regulation (Kooiman et al., 2004; Nemeroff, 2004), thus favoring the emergence of the disorder,
8
9 for example by revealing a pre-existing genetic susceptibility or by interacting with other
10
11 environmental stressors (Caspi & Moffitt, 2006).
12
13
14
15
16

17
18 The elevated CTQ score observed among bipolar patients may also be regarded as a consequence
19
20 of behavioral disturbances associated either with an early onset of the disease, with prodromal
21
22 features (existing before the adulthood onset of bipolar disorder) or with early onset comorbid
23
24 disorders. For example, early onset bipolar disorder has been associated with conduct disorder,
25
26 disruptive behavior disorders (Biederman et al., 2000; Spencer et al., 2001), attention deficit with
27
28 hyperactivity (Kent & Craddock, 2003) and substance abuse comorbidity (Lin et al., 2006). These
29
30 clinical features might induce dysfunctional parental attitudes and this burden is likely to lead to
31
32 inappropriate discipline and in certain conditions to abuse. Furthermore, caregivers of bipolar
33
34 patients exhibit high levels of expressed emotion, including critical, hostile, or over-involved
35
36 attitudes (Heru & Ryan, 2004; Ogilvie, Morant, & Goodwin, 2005; Perlick et al., 1999; Romero,
37
38 Delbello, Soutullo, Stanford, & Strakowski, 2005). Finally, the association between emotional
39
40 abuse and bipolar disorder might be related to parental psychopathological traits. Indeed,
41
42 epidemiological studies have shown that affective disorders and alcoholism are more prevalent
43
44 among relatives of bipolar children than other children (Smoller & Finn, 2003; Todd, Geller,
45
46 Neuman, Fox, & Hickok, 1996). This high prevalence might result in less cohesive and
47
48 organized, and more conflictual families (Chang, Blasey, Ketter, & Steiner, 2001; Romero et al.,
49
50 2005), in turn resulting in an increased likelihood of traumatic events during childhood.
51
52
53
54
55
56
57
58
59
60

1
2
3 Childhood trauma, in particular emotional abuse, has also been reported in recurrent
4
5 unipolar depression (Bernet & Stein, 1999; Moskvina et al., 2007), thus our results are probably
6
7 not specific to bipolar disorder. This potentially shared environmental factor has been supposed
8
9 to be associated with heightened emotional stress reactivity (Glaser, van Os, Portegijs, & Myin-
10
11 Germeys, 2006), that might be a common feature between bipolar disorder and unipolar recurrent
12
13 depression (Hlastala et al., 2000; Myin-Germeys et al., 2003). Our findings may shed some light
14
15 on common psychopathological dimensions in unipolar and bipolar disorders in relation with
16
17 shared early environmental stressors. This remains speculative and should be formally tested in
18
19 samples including both bipolar and unipolar patients.
20
21
22
23
24
25
26

27 If confirmed, the preferential association between childhood emotional abuse and bipolar
28
29 affective disorder during adulthood may have several clinical implications. First, histories of
30
31 childhood trauma required to be routinely assessed in clinical practice among bipolar patients.
32
33 Unless trauma histories are systematically assessed, they are unlikely to come to the attention of
34
35 treatment professionals (Bernstein & Fink, 1998). A systematic assessment may dramatically
36
37 improve the detection of such traumatic events.
38
39
40
41
42

43 The potential therapeutic implications are of major importance (Celano & Rothbaum,
44
45 2002; Putnam & Hulsmann, 2002). First, trauma-focused psychotherapies, using different
46
47 theoretical models, have been suggested to produce clinical benefits in different subgroups of
48
49 patients with history of childhood abuse (Azar & Weinzierl, 2005; Callahan, Price, & Hilsenroth,
50
51 2004; Celano & Rothbaum, 2002; Mueser et al., 2007; Price, Hilsenroth, Petretic-Jackson, &
52
53 Bonge, 2001; Wheeler, 2007). To date, no substantial evidence exists that such treatment
54
55 modalities are effective in bipolar patients with prior abuse and further researches are required in
56
57
58
59
60

1
2
3 this field. Since childhood trauma are supposed to increase stress sensitivity and reactivity
4
5 (Glaser et al., 2006; Heim et al., 2000; Shack, Averill, Kopecky, Krajewski, & Gummattira,
6
7 2004), we may postulate that some psychotherapeutic approaches might target these potential late
8
9 consequences of early trauma. This is of great interest since stress reactivity was supposed to be
10
11 associated with a greater proneness toward relapses (Hlastala et al., 2000; Myin-Germeys et al.,
12
13 2003; Post & Leverich, 2006). However, such hypothesis requires further investigation.
14
15
16
17
18
19

20 Conclusion

21
22
23
24
25 Bipolar patients reported more frequent and more severe forms of childhood trauma than
26
27 controls. This result suggests that childhood trauma might represent a risk factor to bipolar
28
29 disorder, although without definitively demonstrated causality. These findings involve that
30
31 clinicians should be aware of such environmental risk factors and routinely evaluate histories of
32
33 childhood trauma among bipolar patients. This potentially leads to trauma-focused therapeutic
34
35 interventions in patients with such past history. We report for the first time a preferential
36
37 implication and a dose-effect of childhood emotional abuse in bipolar patients, which may
38
39 represent either a specific risk factor or a characteristic correlated with other risk factors in
40
41 offspring such as familial/genetic susceptibility factors or parental psychopathology. Further
42
43 case-control studies and high risk studies are required to replicate these findings and to
44
45 investigate the preferential implication of emotional abuse in bipolar disorder.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

- American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington DC.
- Azar, S. T., & Weinzierl, K. M. (2005). Child maltreatment and childhood injury research: a cognitive behavioral approach. *Journal of Pediatric Psychology, 30*, 598-614.
- Bech, P., Rafaelsen, O. J., Kramp, P., & Bolwig, T. G. (1978). The mania rating scale: scale construction and inter-observer agreement. *Neuropharmacology, 17*, 430-431.
- Bernet, C. Z., & Stein, M. B. (1999). Relationship of childhood maltreatment to the onset and course of major depression in adulthood. *Depression and Anxiety, 9*, 169-174.
- Bernstein, D. P., & Fink, L. (1998). *Childhood Trauma Questionnaire : a retrospective self-report - Manual*. San Antonio: The psychological Corporation - Harcourt Brace and Company.
- Bernstein, D. P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., et al. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American Journal of Psychiatry, 151*, 1132-1136.
- Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., et al. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse & Neglect, 27*, 169-190.
- Biederman, J., Mick, E., Faraone, S. V., Spencer, T., Wilens, T. E., & Wozniak, J. (2000). Pediatric mania: a developmental subtype of bipolar disorder ? *Biological Psychiatry, 48*, 458-466.
- Bremner, J. D. (2002). Neuroimaging of childhood trauma. *Seminars in Clinical Neuropsychiatry, 7*, 104-112.
- Brown, G. R., McBride, L., Bauer, M. S., & Williford, W. O. (2005). Impact of childhood abuse

1
2
3 on the course of bipolar disorder: a replication study in U.S. veterans. *Journal of Affective*
4
5
6 *Disorders*, 89, 57-67.

7
8 Callahan, K. L., Price, J. L., & Hilsenroth, M. J. (2004). A review of interpersonal-
9
10 psychodynamic group psychotherapy outcomes for adult survivors of childhood sexual abuse.
11
12 *International Journal of Group Psychotherapy*, 54, 491-519.

13
14 Carballo, J. J., Harkavy-Friedman, J., Burke, A. K., Sher, L., Baca-Garcia, E., Sullivan, G. M., et
15
16 al. (2008). Family history of suicidal behavior and early traumatic experiences: additive effect on
17
18 suicidality and course of bipolar illness ? *Journal of Affective Disorders*, 109, 57-63.

19
20 Caspi, A., & Moffitt, T. E. (2006). Gene-environment interactions in psychiatry: joining forces
21
22 with neuroscience. *Nature Reviews Neuroscience*, 7, 583-590.

23
24
25
26 Celano, M., & Rothbaum, B. O. (2002). Psychotherapeutic approaches with survivors of
27
28 childhood trauma. *Seminars in Clinical Neuropsychiatry*, 7, 120-128.

29
30
31 Chang, K. D., Blasey, C., Ketter, T. A., & Steiner, H. (2001). Family environment of children
32
33 and adolescents with bipolar parents. *Bipolar Disorders*, 3, 73-78.

34
35
36 Cohen, A. N., Hammen, C., Henry, R. M., & Daley, S. E. (2004). Effects of stress and social
37
38 support on recurrence in bipolar disorder. *Journal of Affective Disorders*, 82, 143-147.

39
40
41 Etain, B., Henry, C., Bellivier, F., Mathieu, F., & Leboyer, M. (2008). Beyond Genetics:
42
43 Childhood Affective Trauma in Bipolar Disorder. *Bipolar Disorders*, 10, 867-876.

44
45
46 Garno, J. L., Goldberg, J. F., Ramirez, P. M., & Ritzler, B. A. (2005). Impact of childhood abuse
47
48 on the clinical course of bipolar disorder. *British Journal of Psychiatry*, 186, 121-125.

49
50
51 Glaser, J. P., van Os, J., Portegijs, P. J., & Myin-Germeys, I. (2006). Childhood trauma and
52
53 emotional reactivity to daily life stress in adult frequent attenders of general practitioners.
54
55 *Journal of Psychosomatic Research*, 61, 229-236.

56
57
58 Hammersley, P., Dias, A., Todd, G., Bowen-Jones, K., Reilly, B., & Bentall, R. P. (2003).
59
60

1
2
3 Childhood trauma and hallucinations in bipolar affective disorder: preliminary investigation.

4
5 *British Journal of Psychiatry*, 182, 543-547.

6
7
8 Heim, C., & Nemeroff, C. B. (2001). The role of childhood trauma in the neurobiology of mood

9
10 and anxiety disorders: preclinical and clinical studies. *Biological Psychiatry*, 49, 1023-1039.

11
12 Heim, C., Newport, D. J., Heit, S., Graham, Y. P., Wilcox, M., Bonsall, R., et al. (2000).

13
14 Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in

15
16 childhood. *JAMA : the Journal of the American Medical Association*, 284, 592-597.

17
18 Heim, C., Newport, D. J., Wagner, D., Wilcox, M. M., Miller, A. H., & Nemeroff, C. B. (2002).

19
20 The role of early adverse experience and adulthood stress in the prediction of neuroendocrine

21
22 stress reactivity in women: a multiple regression analysis. *Depression and Anxiety*, 15, 117-125.

23
24 Heru, A. M., & Ryan, C. E. (2004). Burden, reward and family functioning of caregivers for

25
26 relatives with mood disorders: 1-year follow-up. *Journal of Affective Disorders*, 83, 221-225.

27
28 Hlastala, S. A., Frank, E., Kowalski, J., Sherrill, J. T., Tu, X. M., Anderson, B., et al. (2000).

29
30 Stressful life events, bipolar disorder, and the "kindling model". *Journal of Abnormal*

31
32 *Psychology*, 109, 777-786.

33
34
35
36
37
38 Hyun, M., Friedman, S. D., & Dunner, D. L. (2000). Relationship of childhood physical and

39
40 sexual abuse to adult bipolar disorder. *Bipolar Disorders*, 2, 131-135.

41
42
43 Johnson, S. L., & Roberts, J. E. (1995). Life events and bipolar disorder: implications from

44
45 biological theories. *Psychological Bulletin*, 117, 434-449.

46
47
48 Kent, L., & Craddock, N. (2003). Is there a relationship between attention deficit hyperactivity

49
50 disorder and bipolar disorder? *Journal of Affective Disorders*, 73, 211-221.

51
52
53 Kooiman, C. G., van Rees Vellinga, S., Spinhoven, P., Draijer, N., Trijsburg, R. W., &

54
55 Rooijmans, H. G. (2004). Childhood adversities as risk factors for alexithymia and other aspects

56
57 of affect dysregulation in adulthood. *Psychotherapy and Psychosomatics*, 73, 107-116.

58
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- Leverich, G. S., McElroy, S. L., Suppes, T., Keck, P. E., Jr., Denicoff, K. D., Nolen, W. A., et al. (2002). Early physical and sexual abuse associated with an adverse course of bipolar illness. *Biological Psychiatry*, *51*, 288-297.
- Leverich, G. S., & Post, R. M. (2006). Course of bipolar illness after history of childhood trauma. *Lancet*, *367*, 1040-1042.
- Lin, P. I., McInnis, M. G., Potash, J. B., Willour, V., MacKinnon, D. F., DePaulo, J. R., et al. (2006). Clinical correlates and familial aggregation of age at onset in bipolar disorder. *American Journal of Psychiatry*, *163*, 240-246.
- Maguire, C., McCusker, C. G., Meenagh, C., Mulholland, C., & Shannon, C. (2008). Effects of trauma on bipolar disorder: the mediational role of interpersonal difficulties and alcohol dependence. *Bipolar Disorders*, *10*, 293-302.
- Meyer, I. H., Muenzenmaier, K., Cancienne, J., & Struening, E. (1996). Reliability and validity of a measure of sexual and physical abuse histories among women with serious mental illness. *Child Abuse & Neglect*, *20*, 213-219.
- Montgomery, S. A., & Asberg, M. (1979). A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, *134*, 382-389.
- Moskvina, V., Farmer, A., Swainson, V., O'Leary, J., Gunasinghe, C., Owen, M., et al. (2007). Interrelationship of childhood trauma, neuroticism, and depressive phenotype. *Depression and Anxiety*, *24*, 163-168.
- Mueser, K. T., Bolton, E., Carty, P. C., Bradley, M. J., Ahlgren, K. F., Distaso, D. R., et al. (2007). The Trauma Recovery Group: a cognitive-behavioral program for post-traumatic stress disorder in persons with severe mental illness. *Community Mental Health Journal*, *43*, 281-304.
- Myin-Germeys, I., Peeters, F., Havermans, R., Nicolson, N. A., DeVries, M. W., Delespaul, P., et al. (2003). Emotional reactivity to daily life stress in psychosis and affective disorder: an

1
2
3 experience sampling study. *Acta Psychiatrica Scandinavica*, 107, 124-131.

4
5 Nemeroff, C. B. (2004). Neurobiological consequences of childhood trauma. *The Journal of*
6
7
8
9 *Clinical Psychiatry*, 65 Suppl 1, 18-28.

10
11 Nurnberger, J. I., Jr., Blehar, M. C., Kaufmann, C. A., York-Cooler, C., Simpson, S. G.,
12
13 Harkavy-Friedman, J., et al. (1994). Diagnostic interview for genetic studies. Rationale, unique
14
15 features, and training. NIMH Genetics Initiative. *Archives of General Psychiatry*, 51, 849-859.

16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
Ogilvie, A. D., Morant, N., & Goodwin, G. M. (2005). The burden on informal caregivers of
people with bipolar disorder. *Bipolar Disorders*, 7 Suppl 1, 25-32.

Otte, C., Neylan, T. C., Pole, N., Metzler, T., Best, S., Henn-Haase, C., et al. (2005). Association
between childhood trauma and catecholamine response to psychological stress in police academy
recruits. *Biological Psychiatry*, 57, 27-32.

Paivio, S. C., & Cramer, K. M. (2004). Factor structure and reliability of the Childhood Trauma
Questionnaire in a Canadian undergraduate student sample. *Child Abuse & Neglect*, 28, 889-904.

Paquette, D., Laporte, L., Bigras, M., & Zoccolillo, M. (2004). Validation of the French version
of the CTQ and prevalence of the history of maltreatment. *Santé Mentale au Québec*, 29, 201-
220.

Paykel, E. S. (2003). Life events and affective disorders. *Acta Psychiatrica Scandinavica*
Supplementum, 418, 61-66.

Perlick, D., Clarkin, J. F., Sirey, J., Raue, P., Greenfield, S., Struening, E., et al. (1999). Burden
experienced by care-givers of persons with bipolar affective disorder. *British Journal of*
Psychiatry, 175, 56-62.

Post, R. M. (1992). Transduction of psychosocial stress into the neurobiology of recurrent
affective disorder. *American Journal of Psychiatry*, 149, 999-1010.

Post, R. M., & Leverich, G. S. (2006). The role of psychosocial stress in the onset and

1
2
3 progression of bipolar disorder and its comorbidities: the need for earlier and alternative modes
4
5 of therapeutic intervention. *Development and Psychopathology*, 18, 1181-1211.

6
7
8 Preisig, M., Fenton, B. T., Matthey, M. L., Berney, A., & Ferrero, F. (1999). Diagnostic
9
10 interview for genetic studies (DIGS): inter-rater and test-retest reliability of the French version.
11
12 *European Archives of Psychiatry and Clinical Neuroscience*, 249, 174-179.

13
14
15 Price, J. L., Hilsenroth, M. J., Petretic-Jackson, P. A., & Bonge, D. (2001). A review of
16
17 individual psychotherapy outcomes for adult survivors of childhood sexual abuse. *Clinical*
18
19 *Psychology Review*, 21, 1095-1121.

20
21
22 Putnam, F. W., & Hulsmann, J. E. (2002). Pharmacotherapy for survivors of childhood trauma.
23
24 *Seminars in Clinical Neuropsychiatry*, 7, 129-136.

25
26
27 Read, J., van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and
28
29 schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica*
30
31 *Scandinavica*, 112, 330-350.

32
33
34 Romero, S., Delbello, M. P., Soutullo, C. A., Stanford, K., & Strakowski, S. M. (2005). Family
35
36 environment in families with versus families without parental bipolar disorder: a preliminary
37
38 comparison study. *Bipolar Disorders*, 7, 617-622.

39
40
41 Roy, A. (2002). Self-rated childhood emotional neglect and CSF monoamine indices in abstinent
42
43 cocaine-abusing adults: possible implications for suicidal behavior. *Psychiatry Research*, 112,
44
45 69-75.

46
47
48 Rush, A. J. (2003). Toward an understanding of bipolar disorder and its origin. *Journal of*
49
50 *Clinical Psychiatry*, 64 Suppl 6, 4-8.

51
52
53 Shack, A. V., Averill, P. M., Kopecky, C., Krajewski, K., & Gummattira, P. (2004). Prior history
54
55 of physical and sexual abuse among the psychiatric inpatient population: a comparison of males
56
57 and females. *The Psychiatric Quartely*, 75, 343-359.

1
2
3 Smoller, J. W., & Finn, C. T. (2003). Family, twin, and adoption studies of bipolar disorder.
4
5 *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, 123, 48-58.
6
7

8 Smoller, J. W., & Gardner-Schuster, E. (2007). Genetics of bipolar disorder. *Current Psychiatry*
9
10 *Reports*, 9, 504-511.
11

12 Spencer, T. J., Biederman, J., Wozniak, J., Faraone, S. V., Wilens, T. E., & Mick, E. (2001).

13 Parsing pediatric bipolar disorder from its associated comorbidity with the disruptive behavior
14
15 disorders. *Biological Psychiatry*, 49, 1062-1070.
16
17

18 Todd, R. D., Geller, B., Neuman, R., Fox, L. W., & Hickok, J. (1996). Increased prevalence of
19
20 alcoholism in relatives of depressed and bipolar children. *Journal of the American Academy of*
21
22 *Child and Adolescent Psychiatry*, 35, 716-724.
23
24
25

26 Wheeler, K. (2007). Psychotherapeutic strategies for healing trauma. *Perspectives in Psychiatric*
27
28 *Care*, 43, 132-141.
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1 : Demographic and clinical characteristics of bipolar patients ($n = 206$) and control subjects ($n = 94$)

Group	Bipolar patients	Control subjects
Sex ratio (men/women) *	0.69 (84/122)	1.61 (58/36)
Age at interview $M (SD)$	41.7 (12.6)	41.2 (11.9)
Bipolar disorder type I	75.2%	0%
Age at onset $M (SD)$	23.9 (9.3)	-
Duration of illness $M (SD)$	17.8 (11.2)	-
Family history of bipolar disorder	46.9%	0%
Psychotic symptoms (lifetime presence)	57.1%	0%
Suicide attempt (lifetime presence)	40%	0%
Panic disorder (with or without agoraphobia)	19.9%	0%
Social phobia	10.4%	0%
Generalized anxiety disorder	10.8 %	0%
Alcohol or cannabis abuse/dependence	30.7%	0%

* $p < .0001$

The presence of posttraumatic stress disorder is not available (absence of specific section in the French version of the DIGS)

Table 2 : Comparison between bipolar patients ($n = 206$) and controls ($n = 94$) for the prevalence of each childhood trauma subtype categorized along a gradient of 4 severity levels

Trauma subtype	Group	None	Low	Moderate	Severe	p_{exact}
Emotional neglect	Bipolar	15.53%	45.63%	22.82%	16.02%	.03
	Controls	23.40%	54.26%	14.89%	7.45%	
Emotional abuse	Bipolar	50.97%	24.27%	9.71%	15.05%	3.10^{-5}
	Controls	76.60%	18.09%	3.19%	2.12%	
Physical neglect	Bipolar	72.81%	17.48%	5.34%	4.37%	.01
	Controls	87.23%	7.45%	5.32%	0.00%	
Physical abuse	Bipolar	77.67%	12.14%	5.34%	4.85%	.04
	Controls	91.49%	5.32%	2.13%	1.06%	
Sexual abuse	Bipolar	68.93%	11.17%	9.71%	10.19%	.10
	Controls	80.86%	9.57%	6.38%	3.19%	

Table 3 : Spearman correlations among the five trauma subtypes in the whole sample (pooling bipolar patients and controls, $N = 300$)

Trauma subtypes	Emotional abuse	Physical neglect	Physical abuse	Sexual abuse
Emotional neglect	.51 **	.50**	.31 **	.18 *
Emotional abuse	-	.39 **	.53 *	.38 **
Physical neglect	-	-	.30 **	.21 *
Physical abuse	-	-	-	.44 **

** $p < .0001$; * $p < .002$

Table 4: Results of logistic regressions testing for an association between disease status and the five trauma subtypes

	Simple logistic regression				Multiple logistic regression (-2 log L) = 340.59						
	<i>B</i>	<i>SE B</i>	<i>p value</i>	-2 <i>Log L</i>	Crude OR	95% CI	<i>B</i>	<i>SE B</i>	<i>p value</i>	Adjusted OR*	95% CI
Emotional neglect	0.44	0.15	.003	362.04	1.56	1.16-2.08	0.08	0.18	.63	1.09	0.77-1.54
Emotional abuse	0.76	0.18	<.0001	346.98	2.15	1.52-3.04	0.63	0.21	.003	1.88	1.23-2.86
Physical neglect	0.57	0.23	.01	365.26	1.77	1.13-2.78	0.25	0.25	.32	1.28	0.79-2.10
Physical abuse	0.65	0.25	.01	363.95	1.92	1.17-3.16	0.02	0.31	.95	1.02	0.56-1.88
Sexual abuse	0.39	0.16	.01	362.88	1.47	1.09-2.00	0.16	0.18	.36	1.18	0.83-1.67

* *Adjusted OR correspond to the stratified estimate of the odds ratio adjusted for the four other CTQ traumas.*

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

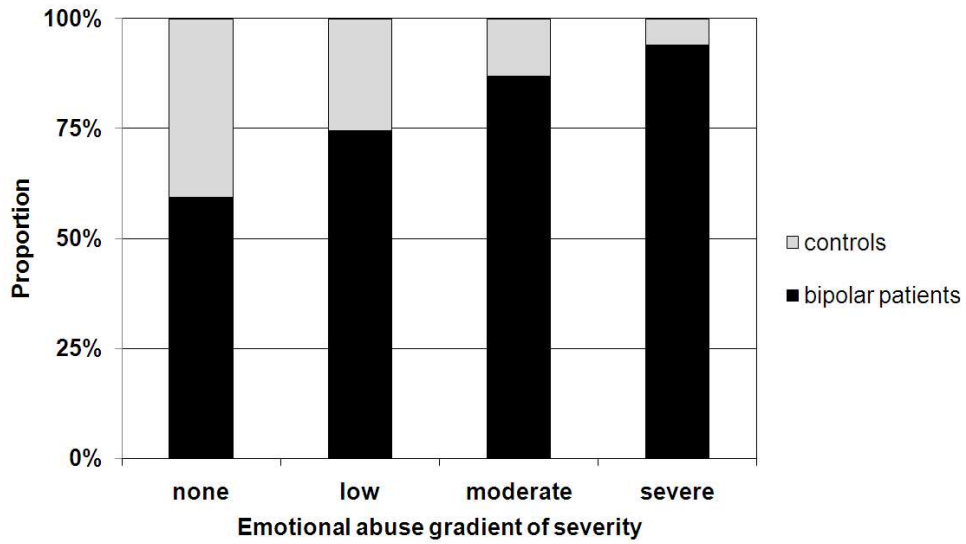


Figure 1 : Proportion of bipolar patients (n = 206) and controls (n = 94) for each emotional abuse severity level (none, low, moderate, severe)
305x174mm (96 x 96 DPI)